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L12: Entry 1 of 6

File: PGPB

Sep 5, 2002

PGPUB-DOCUMENT-NUMBER: 20020123505

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020123505 A1

TITLE: Medical devices containing rapamycin analogs

PUBLICATION-DATE: September 5, 2002

## INVENTOR-INFORMATION:

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US-CL-CURRENT: [514/291](#); [424/426](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
Draw Desc	Image										

☐ 2. Document ID: US 20020012694 A1

L12: Entry 2 of 6

File: PGPB

Jan 31, 2002

PGPUB-DOCUMENT-NUMBER: 20020012694

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020012694 A1

TITLE: TRANSDERMAL ADMINISTRATION OF MENT

PUBLICATION-DATE: January 31, 2002

## INVENTOR-INFORMATION:

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US-CL-CURRENT: [424/449](#); [424/400](#)

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
Draw Desc	Image										

☐ 3. Document ID: US 5362497 A

L12: Entry 3 of 6

File: USPT

Nov 8, 1994

US-PAT-NO: 5362497

DOCUMENT-IDENTIFIER: US 5362497 A

TITLE: Transdermal therapeutic composition

DATE-ISSUED: November 8, 1994

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
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US-CL-CURRENT: 424/449; 424/443, 424/445, 424/447, 424/484, 424/485, 424/487,  
424/488, 514/777, 514/781, 514/944, 514/946, 514/953, 514/964

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
Draw Desc	Image										

☐ 4. Document ID: US 4956181 A

L12: Entry 4 of 6

File: USPT

Sep 11, 1990

US-PAT-NO: 4956181

DOCUMENT-IDENTIFIER: US 4956181 A

TITLE: Nitrate therapy for angina pectoris

DATE-ISSUED: September 11, 1990

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bayer; Gerald W.	Rochester	NY		
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US-CL-CURRENT: 424/448; 424/447

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
Draw Desc	Image									

☐ 5. Document ID: US 4921695 A

L12: Entry 5 of 6

File: USPT

May 1, 1990

US-PAT-NO: 4921695

DOCUMENT-IDENTIFIER: US 4921695 A

TITLE: Antianginal plate for treating ischemic heart disease

DATE-ISSUED: May 1, 1990

## INVENTOR-INFORMATION:

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Babaian; Eduard A.	Moscow			SU
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Utyamyshev; Rustam I.	Moscow			SU
Khromov; Gennady L.	Moscow			SU
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Vikhert; Anatoly M.	Moscow			SU
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Piotrovsky; Vladimir K.	Moscow			SU
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US-CL-CURRENT: 424/449; 424/435, 424/78.27

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KMMC

☐ 6. Document ID: US 4842854 A

L12: Entry 6 of 6

File: USPT

Jun 27, 1989

US-PAT-NO: 4842854

DOCUMENT-IDENTIFIER: US 4842854 A

TITLE: Antianginal plate for treating ischemic heart disease

DATE-ISSUED: June 27, 1989

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Metelitsa; Vladimir I.	Moscow			SU
Vikhert; Anatoly M.	Moscow			SU
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Piotrovsky; Vladimir K.	Moscow			SU
Novikova; Elizaveta B.	Moscow			SU

US-CL-CURRENT: 424/78.18; 424/435, 424/78.24

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KMMC

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L12: Entry 3 of 6

File: USPT

Nov 8, 1994

DOCUMENT-IDENTIFIER: US 5362497 A

TITLE: Transdermal therapeutic composition

Brief Summary Text (14):

As the super water-absorbent resin "ingredient (iv)", mention is made of such resins which are capable of absorbing water of several tens to more than one thousand times as much as its own weight, forming a hydrogel by swelling with water and not releasing water even under elevated pressure. Practical examples include saponified vinyl acetate-acrylic acid ester copolymers, polyacrylates, cross-linked polyvinyl alcohol-maleic anhydride copolymers, cross-linked isobutylene-maleic acid copolymers, saponified polyacrylonitrile graft polymers, starch-acrylic acid graft polymers. Among them, polymers which are capable of absorbing water of about 50 to 2000 times as much as their own weight are preferable. The amount of a super water-absorbent resin to be incorporated into a transdermal therapeutic composition is optional, but, preferably, about 0.1 to 10% (W/W), more preferably, about 0.5 to 5% (W/W).

Brief Summary Text (27):

The transdermal therapeutic composition of this invention is provided in such dosage forms as patch, cataplasma, ointment (inclusive of cream), hard ointment, tape, suppository, lotion, solution, suspension, emulsion and aerosol mist. Among them, transdermal therapeutic plasters (e.g. patch, cataplasma, hard ointment, tape, etc.) are preferable. The ointment (inclusive of cream), suppository, lotion, solution, suspension, emulsion and aerosol can be manufactured by formulating the above-mentioned ingredients (i), (ii), (iii) and (iv), and, if necessary, the nonionic surfactant, inorganic base and acid, with a solvent, suspending agent, emulsifier, propellant, ointment base, suppository base, or the like, which are well known in pharmaceutical industry. If necessary, a preservative (for example, ethyl p-hydroxybenzoate, benzalkonium chloride), antiphlogistic agent (for example, glycyrrhizinoic acid), etc. can be further incorporated. The plasters such as patch, cataplasma, hard ointment and tape can be manufactured by mixing the above-mentioned ingredients (i), (ii), (iii) and (iv), and, when necessary, the nonionic surfactant, inorganic base or acid, with a base which is well known in pharmaceutical industry and, if necessary, after addition of a preservative, an antiphlogistic agent, etc., subjecting the mixture to absorption into, or adhesive to, an appropriate support material. The support material may be a high polymer film, a web of woven or nonwoven fabric, a sheet of paper or the like. The adhesive agent to be used in the manufacture of the patch, cataplasma or tape includes, among others, polyalkyl vinyl ether, polyalkyl acrylate (JP-B-58-23846), polyisobutylene, natural rubber and synthetic rubber adhesives. For assuring suitable plasticity and tackiness, animal oil (for example, squalene, squalane, etc.) or vegetable oil (for example, olive oil, jojoba oil, etc.), petrolatum, lanolin, etc. may be added.

Brief Summary Text (28):

In the manufacture of the ointment, hard ointment, suppository, tape, patch and cataplasma, there may be incorporated ingredients for modulating the transdermal absorption, such as lecithin and other phospholipids, solid paraffin, bees-wax, carnauba wax, hydrogenated castor oil, lanolin, petrolatum, polyvinyl alcohol, polyvinylpyrrolidone, polyethylene glycol, glycerol fatty acid ester, cholesterol, Carbopol, carboxymethylcellulose, carboxyethylcellulose, silicone resin and a lower alcohol (for example, ethanol, isopropyl alcohol, etc.).

Detailed Description Text (5):

First, an aqueous phase was prepared by mixing and dissolving 10 g of Compound (I), i.e. (R)-3-[(S)-1-carboxy-5-(4-piperidyl)pentyl]amino-4-oxo-2,3,4,5-tetrahydro-1,5-benzothiazepine-5-acetic acid, an angiotensin converting enzyme inhibitor, 50 ml of water, 20 g of propylene glycol, 1.15 g of NaOH and 1 g of a super water-absorbent resin [a vinyl acetate-acrylic acid ester copolymer hydrolyzate (Sumikagel SP-510, manufactured by Sumitomo Chemical Co., Ltd.)]. On the other hand, an oily phase was prepared by mixing and dissolving, in ethyl acetate, 43 g of a purified polymer fraction of polyalkyl acrylate adhesive [methyl acrylate-2-ethylhexyl acrylate copolymer emulsion, Nikasol TS-620, manufactured by Nippon Carbide Industries, Co., Ltd.], 5 g of Tween 80 and 20 g of isopropyl myristate. The above aqueous and oily phases were combined and mixed well, and a polyethylene sheet was coated with the mixture in a coverage corresponding to a dry thickness of about 100 .mu.m and dried at 80.degree. C. for 5 minutes. After drying, the coated sheet was covered with a separator (a release sheet) to provide a transdermal therapeutic plaster (tape).

Detailed Description Text (12):

First, an aqueous phase was prepared by mixing and dissolving 15 g of the same Compound (I) as used in Example 1, 70 ml of water, 15 g of propylene glycol, 10 g of 1,3-butylene glycol, 1.15 g of NaOH and 2 g of a super water-absorbent resin [a vinyl acetate-acrylic acid ester copolymer hydrolyzate, Sumikagel SP-510, Sumitomo Chemical Co., Ltd.]. On the other hand, an oily phase was prepared by dissolving, in ethyl acetate, 38 g of polyalkyl vinyl ether adhesive [polyvinyl ethyl ether (Tg:-30.degree. C.)/polyvinyl ethyl ether (Tg:-60.degree. C.)=60parts/40 parts], 5 g of Tween 80 and 15 g of isopropyl myristate. The above aqueous and oily phases were combined and mixed well, and a polyethylene sheet was coated with the mixture in the coverage corresponding to a dry thickness of about 100 .mu.m and dried at 100.degree. C. for 3 minutes. After drying, the coated sheet was covered with a separator to provide a transdermal therapeutic plaster (tape).

Detailed Description Text (26):

An aqueous phase was prepared by mixing and dissolving 15 g of such Compound (I), 30 ml of water, 20 g of propylene glycol, 1.3 g of NaOH and 1 g of a super water-absorbent resin [a vinyl acetate-acrylic acid ester copolymer hydroclyzate (Sumikagel SP-510, manufactured by Sumitomo Chemical Co., Ltd.)]. On the other hand, an oily phase was prepared by mixing and dissolving, in ethyl acetate, 37.7 g of a polyalkyl acrylate adhesive [a copolymer prepared by polymerization of 55 weight parts of 2-ethylhexyl acrylate, 30 weight parts of methoxyethyl acrylate and 15 weight parts of vinyl acetate using ethyl acetate as a Solvent], 5 g of Tween 80 and 20 g of isopropyl myristate. The above aqueous and oily phases were combined and mixed well, and a polyethylene sheet was coated with the mixture in a coverage corresponding to a dry thickness of about 100 .mu.m and dried at 70.degree. C. for 5 minutes. After drying, the coated sheet was covered with a separator (a release sheet) to provide a transdermal therapeutic plaster (tape).

## CLAIMS:

1. A transdermal therapeutic composition which comprises:

(i) 0.1 to 20% of a pharmaceutically effective ingredient;

(ii) 1 to 50% (w/w) water-soluble substance which enhances transdermal absorption of the pharmaceutically effective ingredient;

(iii) 0.1 to 80% (w/w) fat-soluble substance which enhances transdermal absorption of the pharmaceutically effective ingredient; and

(iv) 0.1 to 10% (w/w) vinyl acetate-acrylic acid ester copolymer hydrolyzate capable of absorbing about 50 to 2000 times its own weight of water, whereby upon contact with said water swells to form a hydrogel.

10. A transdermal therapeutic composition according to claim 1, which contains (i) (R)-3-[(S)-1-carboxy-5-(4piperidyl)pentyl]amino-4-oxo-2,3,4,5-tetrahydro-1

,5-benzothiazepine-5-acetic acid, (ii) propylene glycol, (iii) isopropyl myristate, (iv) a vinyl acetate-acrylic acid ester copolymer hydrolyzate, (v) an inorganic base and water.

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L13: Entry 7 of 9

File: USPT

Sep 3, 1991

DOCUMENT-IDENTIFIER: US 5045553 A

TITLE: Pharmaceutical composition for percutaneous drug absorption and percutaneous drug absorption promoter

Drawing Description Text (2):

FIG. 1 is a sectional view schematically illustrating a patch preparation the drug release from which is controlled by means of a sustained release matrix;

Drawing Description Text (3):

FIG. 2 is a sectional view schematically illustrating a patch preparation the drug release from which is controlled by means of a sustained release matrix and which is further provided with an adhesive layer;

Drawing Description Text (5):

FIG. 4 is a sectional view schematically illustrating a patch preparation, wherein the drug migration is controlled through membrane permeation;

Drawing Description Text (6):

FIG. 5 is a sectional view schematically illustrating a patch preparation, wherein the drug migration is controlled through membrane permeation and wherein said preparation is further provided with an adhesive layer; and

Drawing Description Text (7):

FIG. 6 is a sectional view schematically illustrating a patch preparation, wherein the adhesive layer contains the chief ingredient and wherein the release of absorption promoter from the sustained release matrix, which is free of the chief ingredient, is controlled through membrane permeation.

Detailed Description Text (10):

When the pharmaceutical composition is to have the form of patches, said composition is spread over a support member (made of cloth or aluminum, for instance) (cf. FIG. 1) and, if necessary, an adhesive layer is provided (cf. FIG. 2).

Detailed Description Text (12):

The pharmaceutical composition for percutaneous drug absorption according to the invention may also be made up into ointments for ordinary use, such as Macrogol ointments, FAPG ointments, hydrophilic ointments, absorptive ointments, Carbopol gel ointments, etc. In this case, for providing sustained release property, controlling drug absorption and preventing adherence to clothes, it is also possible to fill the composition in an appropriate container and attach the container to the skin so that said composition can come into contact therewith or to coat a support member (as in the case of tape preparations) with said composition to a certain thickness and apply the whole to the skin so that said composition can come into contact therewith.

Detailed Description Text (13):

Furthermore, the pharmaceutical composition for percutaneous drug absorption according to the invention can be made up into patches, for example by spreading said composition over an appropriate support member (made of aluminum, for instance) and, if necessary, sealing with an absorption promoter release-controlling film such as an ethylene-vinyl acetate copolymer (EVA) film (cf. FIG. 4), and furthermore, if

necessary, providing an adhesive layer (cf. FIG. 5). With these patches, drug absorption can be controlled by interposing such absorption promoter release controlling film or membrane between said pharmaceutical composition or adhesive layer and the skin so that an effective blood concentration of the chief ingredient can be maintained for a prolonged period of time. The rate of drug absorption can be controlled as desired by adequately modifying the thickness of said absorption promoter release controlling film and/or the composition of the EVA film. Furthermore, the chief ingredient and/or the above-mentioned absorption promoter may be added to the adhesive layer as necessary so that the percutaneous absorbability can be increased and/or the absorption of the chief ingredient can be maintained.

Detailed Description Text (14):

In cases where the pharmaceutical composition for percutaneous drug absorption is made up into patches, it is not always necessary that the chief ingredient and absorption promoter be present in the same layer. Thus, for example, patches may be prepared by spreading a dermatocompatible sustained release matrix free of the chief ingredient over a support member, then sealing with an absorption promoter release controlling film and further providing thereon an adhesive layer containing the chief ingredient (cf. FIG. 6).

Detailed Description Text (18):

The pharmaceutical composition for percutaneous drug absorption according to the invention is preferably made up into patches such as mentioned above.

Detailed Description Text (29):

The suspension gel obtained in Example 6 was spread over a support member made of aluminum in an amount of 40.2 mg per square centimeter. The gel layer was covered with an EVA film (vinyl acetate content 14%, thickness 50 .mu.m). After heat sealing, there was obtained a patch preparation.

Detailed Description Text (31):

A patch preparation was produced by using the solution gel obtained in Example 8 and following the procedure of Example 9.

Detailed Description Text (34):

A patch preparation was produced by using the solution gel obtained in Example 7 and an EVA film (vinyl acetate content 14%, thickness 50 .mu.m) and following the procedure of Example 9. In this example, however, the gel was spread over the aluminum support in an amount of 38.3 mg per square centimeter.

Detailed Description Text (36):

A patch preparation like that obtained in Example 12 was produced by using a 30-.mu.m-thick EVA film having a vinyl acetate content of 14%.

Detailed Description Text (38):

A patch preparation was produced by further forming an acrylic adhesive layer on the EVA film of the patch preparation produced in Example 13. The adhesive layer was prepared from the following components:

Detailed Description Text (42):

The above gel was spread over an aluminum support in an amount of 34 mg of gel per square centimeter. The gel layer was covered with an EVA film (vinyl acetate content 14%, thickness 30 .mu.m), which was heat-sealed. The EVA film was further coated with the adhesive mass prepared as described above. Thus was obtained a patch preparation.

Detailed Description Text (46):

The solution gel obtained in Example 16 was spread over an aluminum support in an amount of 38.3 mg per square centimeter. The gel layer was then covered with an EVA film (vinyl acetate content 14%, thickness 30 .mu.m), followed by heat sealing. Thus was produced a patch preparation.

Detailed Description Text (48):

A patch preparation was produced by using the solution gel obtained in Example 17 and following the treatment procedure of Example 18. The gel was applied to the



aluminum support in an amount of 40.2 mg per square centimeter.

Detailed Description Text (52):

The solution gel was obtained in Example 20 was spread over an aluminum support in an amount of 37.45 mg per square centimeter. The gel layer was covered with an EVA film (vinyl acetate content 14%, thickness 30 .mu.m), followed by heat sealing. A patch preparation was thus produced.

Detailed Description Text (54):

A patch preparation was produced by using the solution gel obtained in Example 21 and following the procedure of Example 22. In this example, however, the gel was applied to the aluminum support in an amount of 39.22 mg per square centimeter.

Detailed Description Paragraph Table (21):

		[C-1] Comparative test with tape preparations			
Test preparations	Tape preparations of	Comparative Example 3	Tape preparation of		
Example 5	Test results Plasma level (ng/ml)	at 1 hour	at 8 hour		
		Comparative Example 3 0.06 .+-. 0.06 0.15			
.+-. 0.03	Example 5	0.66 .+-. 0.05	2.05 .+-. 0.20		
		[C-2] Test with ethanol-and oleic			
acid-containing	<u>patch</u> preparations	Test preparations	<u>Patch</u> of Example 9	<u>Patch</u> of	
Example 10	Test results Test Plasma level (ng/ml)	preparation at 4 hour	at 6 hour		
		Example 9 2.62 3.02 Example 10 3.08 6.97			

Detailed Description Paragraph Table (22):

		[D-1] Test with <u>patches</u> having an adhesive			
layer	Test preparations	<u>Patch</u> of Example 14	<u>Patch</u> of Example 15	Test results	Test
		Plasma level (ng/ml) preparation at 4 hour at 8 hour at 24 hours			
		Example 14 4.33 5.28 2.58 Example 15 0.47			
1.41	0.97	(Each group consisting of 3 dogs.)			
		[D-2] Test with <u>patches</u> Test preparations <u>Patch</u> of Example 13 <u>Patch</u> of Example 18			
		<u>Patch</u> of Example 19 <u>Patch</u> of Example 22 <u>Patch</u> of Example 23			

CLAIMS:

4. A pharmaceutical composition for percutaneous drug absorption as claimed in claim 1, said composition being formulated in the form of a patch.

## WEST Search History

DATE: Friday, September 27, 2002

### Set Name Query

side by side

### Hit Count Set Name

result set

*DB=USPT,PGPB,JPAB,EPAB,DWPI,TDBD; PLUR=YES; OP=OR*

L13	patch and ointment and support adj10 thickness	9	L13
L12	L9 and acrylic adj3 acid	6	L12
L11	L9 and acrylic adj3 acid	0	L11
L10	L9 and modulus	0	L10
L9	ointment adj5 patch and support and vinyl adj1 acetate	141	L9
L8	L7 and modulus	7	L8
L7	transdermal and patch and support and ointment and coat\$	1159	L7
L6	transdermal and patch and support and ointment and coat\$ and vapor adj5 permeability	0	L6
L5	tablet and core and conjugated adj1 estrogen and cellulose and coat\$	50	L5
L4	tablet and core and conjugated adj1 estrogen and cellulose and calcium and coat\$ and sugar	37	L4
L3	moringa and tocopherol and oil and methylene	2	L3
L2	moringa and tocopherol and oil	13	L2
L1	moringa and tocopherol and stability	2	L1

END OF SEARCH HISTORY